General

Guideline Title

IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes.

Bibliographic Source(s)

Game FL, Apelqvist J, Attinger C, Hartemann A, Hinchliffe RJ, LÃ¶ndahl M, Price PE, Jeffcoate WJ, International Working Group on the Diabetic Foot. IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):75-83. [93 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC) and the International Working Group on the Diabetic Foot (IWGDF): For the 2015 IWGDF Guidance documents, the IWGDF invited five working groups of international experts to produce guidance on the prevention and management of foot problems in diabetes. Major recommendations provided in the *IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes* are presented below. See also the NGC summaries of IWGDF guidance on the following related topics:

- Prevention of foot ulcers in at-risk patients with diabetes
- Footwear and offloading to prevent and heal foot ulcers in diabetes
- Diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers in diabetes
- Diagnosis and management of foot infections in persons with diabetes

Definitions for the quality of the evidence (High, Moderate, Low, Very Low) and strength of recommendations (Strong, Weak) are provided at the end of the "Major Recommendations" field.

Recommendations of Specific Types of Ulcer Treatment in the Management of Diabetic Foot Ulcers (Excluding Offloading)

What is the best way of debriding a diabetic foot ulcer?

1. Clean ulcers regularly with clean water or saline, debride them when possible in order to remove debris from the wound surface and dress them with a sterile, inert dressing in order to control excessive exudate and maintain a warm, moist environment in order to promote healing.

(Grading of Recommendations Assessment, Development and Evaluation [GRADE] strength of recommendation: Strong; Quality of evidence: Low)
2. In general, remove slough, necrotic tissue and surrounding callus with sharp debridement in preference to other methods, taking relative contraindications such as severe ischemia into account. (Strong; Low)

What is the best dressing to use?

3. Select dressings principally on the basis of exudate control, comfort and cost. (Strong; Low)
4. Do not use antimicrobial dressings with the goal of improving wound healing or preventing secondary infection. (Strong; Moderate)

Does systemic hyperbaric oxygen therapy hasten wound healing in diabetic foot ulcers?

5. Consider the use of systemic hyperbaric oxygen therapy, even though further blinded and randomized trials are required to confirm its cost-effectiveness, as well as to identify the population most likely to benefit from its use. (Weak; Moderate)

Does topical negative pressure wound therapy (NPWT) hasten healing in diabetic foot ulcers?

6. Topical negative pressure wound therapy may be considered in post-operative wounds even though the effectiveness and cost-effectiveness of the approach remain to be established. (Weak; Moderate)

Is there a place for the use of other topically applied treatments?

7. Do not select agents reported to improve wound healing by altering the biology of the wound, including growth factors, bioengineered skin products and gases, in preference to accepted standards of good quality care. (Strong; Low)

Is there a place for other local therapies to improve wound healing in the diabetic foot?

8. Do not select agents reported to have an impact on wound healing through alteration of the physical environment, including through the use of electricity, magnetism, ultrasound and shockwaves, in preference to accepted standards of good quality care. (Strong; Low)

Is there a place for other systemic therapies, including drugs and herbal therapies, in improving wound healing in the diabetic foot?

9. Do not select systemic treatments reported to improve wound healing, including drugs and herbal therapies, in preference to accepted standards of good quality care. (Strong; Low)

Definitions

Recommendations in this guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the quality of evidence on the risk of bias of included studies, effect sizes, and expert opinion, and rated the quality of evidence as 'high,' 'moderate' or 'low.' They assessed the strength of each recommendation as 'strong' or 'weak,' based on the quality of evidence, balance between benefits and harm, patient values and preferences, and costs (resource utilization). The rationale behind each recommendation is described in the original guideline document. See the GRADE Web site for more information.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Chronic diabetic foot ulcers

Guideline Category

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Podiatry

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Podiatrists

Guideline Objective(s)

To provide recommendations for use of interventions to enhance the healing of chronic ulcers of the foot in diabetes

Target Population

Persons aged 18 years or older with chronic diabetic foot ulcers

Interventions and Practices Considered

1. Debridement
2. Use of wound dressings
3. Systemic hyperbaric oxygen therapy
4. Topical negative pressure wound therapy (NPWT)

Note: The following interventions/practices were considered but not recommended in preference to accepted standards of good quality care: agents reported to improve wound healing by altering the biology of the wound, including growth factors, bioengineered skin products and gases; agents reported to have an impact on wound healing through alteration of the physical environment, including through the use of electricity, magnetism, ultrasound and shockwaves; and systemic treatments reported to improve wound healing, including drugs and herbal therapies.

Major Outcomes Considered

- Ulcer healing
- Time to healing
- Reduction in ulcer area

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Methods

Controlled studies, which were either prospective or retrospective, published in any language, and which evaluated interventions for the treatment of chronic foot ulcers in people aged 18 years or older with either type 1 or type 2 diabetes mellitus were considered. Studies were included if they concerned agents or interventions that may accelerate the healing process, and the primary outcomes used were clinical: healing, time to healing, and/or reduction in ulcer area. Search strategies (see Appendix A of the systematic review [see the "Availability of Companion Documents" field]) included selected search terms on study design, patient group, clinical problem and interventions of interest by using Medline (June 2010 to June 2014) and EMBASE (June 2010 to June 2014). Randomized controlled trials (RCTS), case-control studies, prospective and retrospective cohort studies, control before-and-after and interrupted time series designs were included. Bibliography tracking of identified articles was not performed. Previously performed high-quality systematic reviews and Cochrane reviews on the topics of interest were searched to determine the need for an extension to the literature search. A later search was made of the following clinical trials registries; the search terms used were Foot Ulcer; Diabetes Mellitus; Diabetic Foot Ulcer; and Diabetic Foot: http://www.controlled-trials.com/, www.clinicaltrials.gov, www.who.int/trialsearch, clinicalstudies.info.nih.gov/, cordis.europa.eu/en/home.html, www.clinicaltrialsregister.eu/, www.pactr.org/, www.anzctr.org.au/, www.canadiancancertrials.ca/, www.fmhs.auckland.ac.nz/en/sms/about/our-departments/oncology/cancer-trials-nz.html, www.chictr.org.cn/abouten.aspx, cris.nih.go.kr/cris/en/search/basic_search.jsp, registroclinico.sld.cu/, drks-neu.uniklinik-freiburg.de/drks_web/, www.hkclinicaltrials.com/, www.irct.ir/, www.umin.ac.jp/ctr/, www.kctr.se, clinicaltrials.health.nz/, www.sanctr.gov.za/SAClinicalTrials/tabid/169/Default.aspx, www.slctr.lk/, www.clinicaltrials.in.th/, www.ukctg.nihr.ac.uk/ and www.controlled-trials.com/ukctr/, and attempts were made to contact investigators if there was no evidence of publication of relevant studies.

Two reviewers independently assessed all identified references by title and abstract to determine possible eligibility. Full-paper copies of identified articles were retrieved, and eligibility was confirmed or rejected by one of four pairs of independent reviewers.

Number of Source Documents

In the current 2015 update, a total of 2161 articles were identified: 1501 from Medline and 660 from EMBASE. Forty-three of these were selected for full text review. An additional seven articles were identified from other sources, either other systematic reviews or clinical trial databases. Of the total 50 articles, 33 that fulfilled the inclusion criteria were included in the review (see Figure 1 in the systematic review [see the "Availability of Companion Documents" field]).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Recommendations in the guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the quality of evidence on the risk of bias of included studies, effect sizes, and expert opinion, and rated the quality of evidence as 'high', 'moderate' or 'low'. See the GRADE Web site for more information.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Methods

Each study was scored for methodological quality using scoring lists specific for each study design and based on checklists developed by the Scottish Intercollegiate Guidelines Network (SIGN). Equal weighting was applied to each validity criterion. Findings on data extraction and methodological quality were discussed between co-reviewers and a final decision endorsed by the entire group. Quality items were rated as 'done', 'not done' or 'not reported', and only those rated as 'done' contributed to methodological quality score. This quality score was translated into a level of evidence according to the SIGN instrument: (1) randomized controlled trials (RCTs) and (2) studies with case-control, cohort, control before and after or interrupted time series design. Studies were also rated as ++ (well conducted with very low risk of bias), + (well conducted with low risk of bias) and − (low quality with higher risk of bias). Meta-analyses, other reviews and studies reporting non-analytic case reports and case series were not included. Reviewers did not assess their own work because of potential conflicts of interest.

Extracted data were summarized in evidence tables on a study-by-study narrative basis. Because of the heterogeneity of study designs, including interventions, follow-up and outcomes, no attempt was made to pool the results. The evidence tables were compiled following collective discussion by the working party, and conclusions were drawn. The papers selected for scoring were divided into the same ten categories as the 2012 review, except that the articles on the use of platelet-derived growth factors have now been included in the section on cell therapy (in contrast to the previous allocation to the section on wound biochemistry); the section on oxygen has been expanded to include other gases.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Following the systematic review, the experts in the working group formulated recommendations based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The GRADE system allows the experts to provide a rating for each recommendation based on both the strength with which it is recommended and the quality of the evidence underlying it. In this manner the link is made between scientific evidence and recommendations for daily clinical practice (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Recommendations in the guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the strength of each recommendation as 'strong' or 'weak', based on the quality of evidence, balance between benefits and harm, patient values and preferences, and costs (resource utilization). See the GRADE Web site for more information.

Cost Analysis

Even though there are a small number of studies suggesting efficacy of particular interventions, there are very few studies confirming effectiveness (and, thereby, of cost-effectiveness) of any particular intervention in routine care.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Consensus

The members of the International Working Group on the Diabetic Foot (IWGDF) Editorial Board met in person on a number of occasions to thoroughly review the systematic reviews and the Guidance documents, which were then revised by the working group based on this editorial review. When found satisfactory, the Editorial Board sent the Guidance document to the IWGDF representatives for comments; the editorial board processed all comments received and made changes where needed in collaboration with the chair of the working group.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of interventions to enhance the healing of chronic ulcers of the foot in diabetes

Refer to the discussion sections following each recommendation in the original guideline document for an assessment of balance of benefits and harms for individual recommendations.

Potential Harms

Potential adverse effects of negative pressure wound therapy (NPWT) include wound maceration, retention of dressings and wound infection.

Refer to the discussion sections following each recommendation in the original guideline document for an assessment of balance of benefits and harms for individual recommendations.

Contraindications

Contraindications

Severe ischemia is a relative contraindication to the use of sharp debridement for removing slough, necrotic tissue and surrounding callus.

Qualifying Statements

Qualifying Statements

- The guideline recommendations are derived from critical systematic review of all relevant publications, but this process has its limitations, and these must be borne in mind. The first is that the reviews sought evidence specifically that an intervention may improve healing (and only of foot ulcers complicating diabetes – and not of other wounds, whether acute or chronic). As, however, the process of healing is a highly complex one, involving the interaction of many different cell types and signalling pathways, it is likely that the benefit of the majority of specific interventions is limited to a particular type of wound and to a particular phase in the healing process. As the process tends to last for weeks or months, this means that the impact of any beneficial effect of a therapy may not be apparent. It is also important to consider whether the benefit of a therapy has been demonstrated in people who are also receiving usual best care, including adequate offloading in

those with ulcers on weight-bearing areas of the foot.

- If, however, studies are of insufficient duration to assess complete healing of an ulcer as an outcome measure, it may be possible to use a surrogate measure – such as percentage reduction in wound area over 4 weeks, which has been shown to correlate with, and to be predictive of, the incidence of eventual healing. The adoption of such a surrogate measure will reduce the chance of a short-term response to an intervention being obscured by the complexity of the overall healing process. Demonstration of benefit in such short-duration studies could then be used as the foundation for further work designed to determine the specific population and circumstances in which the use of the intervention is likely to be beneficial.
- Ultimately, however, the clinical endpoint of care is to accelerate complete healing of chronic ulcers of the foot in diabetes, and this must be demonstrated if any treatment is to be generally recommended. Hitherto, such recommendation has not been possible because of the limitations both in extent and, in many cases, in quality of reported studies.
- See also the section "Key unresolved issues" in the original guideline document.

Implementation of the Guideline

Description of Implementation Strategy

Guidelines will be implemented via the training programs of the International Working Group on the Diabetic Foot (IWGDF) as well as with support of the translation of the guidelines in local languages.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Game FL, Apelqvist J, Attinger C, Hartemann A, Hinchliffe RJ, LÃ¶ndahl M, Price PE, Jeffcoate WJ, International Working Group on the Diabetic Foot. IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):75-83. [93 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jan

Guideline Developer(s)

International Working Group on the Diabetic Foot - Nonprofit Organization

Source(s) of Funding

International Working Group on the Diabetic Foot

Guideline Committee

International Working Group on the Diabetic Foot

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

The International Working Group on the Diabetic Foot Guidance is developed by working groups of independent experts. These documents are written without any influence from commercial, political, academic or other interest groups.

Conflicts of Interest

FG, JA, AH, RH, ML, PP, WJ: None declared relating to the interventions reviewed.

CA: Consultant: Acelity, Integra and Smith & Nephew.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Diabetes/Metabolism Research and Reviews Web site .

Availability of Companion Documents

The following are available:

- Game FL, Apelqvist J, Attinger C, Hartemann A, Hinchliffe RJ, Löndahl M, Price PE, Jeffcoate WJ. Effectiveness of interventions to enhance healing of chronic ulcers of the foot in diabetes: a systematic review. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):154-68. Available from the Diabetes/Metabolism Research and Reviews Web site .
- Bakker K, Apvelqvist J, Lipsky BA, Van Netten JJ, Schaper NC, International Working Group on the Diabetic Foot (IWGDF). The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):2-6. Available from the Diabetes/Metabolism Research and Reviews Web site .
- Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K, International Working Group on the Diabetic Foot (IWGDF). Prevention and management of foot problems in diabetes: a summary guidance for daily practice 2015, based on the IWGDF Guidance Documents. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):7-15. Available from the Diabetes/Metabolism Research and Reviews Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on November 4, 2016. The information was verified by the guideline developer on December 11, 2016.

Copyright Statement

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